

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
21 May 2004 (21.05.2004)

PCT

(10) International Publication Number  
**WO 2004/042024 A2**

(51) International Patent Classification<sup>7</sup>:

C12N

(21) International Application Number:

PCT/US2003/034826

(22) International Filing Date: 31 October 2003 (31.10.2003)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

60/423,262

1 November 2002 (01.11.2002)

US

(71) Applicant (for all designated States except US): **THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA** [US/US]; 3160 Chestnut Street, Suite 200, Philadelphia, PA 19104 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **REICH, Samuel, Jotham** [US/US]; 312 Kent Road, Bala Cynwyd, PA 19004 (US). **SURACE, Enrico, Maria** [IT/IT]; Largo Della, Crocetta 2, I-20122 Milan (IT). **TOLENTINO, Michael, J.** [US/US]; 474 South Ithan Avenue, Villanova, PA 19085 (US).

(74) Agents: **FRANK, George, A.** et al.; Drinker Biddle & Reath LLP, One Logan Square, 18th and Cherry Streets, Philadelphia, PA 19103-6996 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

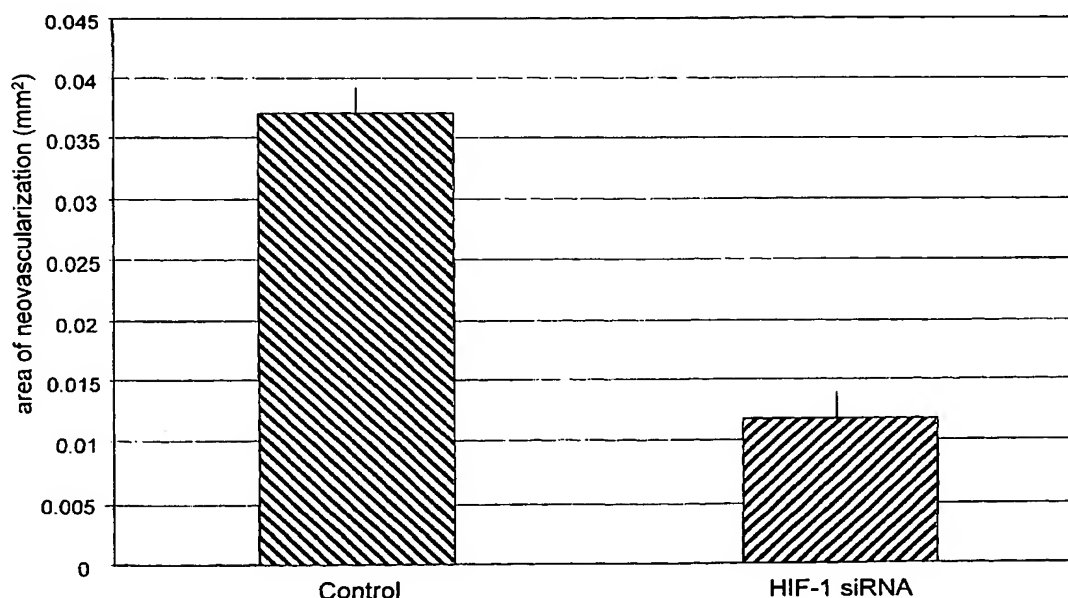
(84) Designated States (*regional*): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— without international search report and to be republished upon receipt of that report

[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR siRNA INHIBITION OF HIF-1 ALPHA



(57) Abstract: RNA interference using small interfering RNAs which target HIF-1 alpha mRNA inhibit expression of the HIF-1 alpha gene. As HIF-1 alpha is a transcriptional regulator of VEGF, expression of VEGF is also inhibited. Control of VEGF production through siRNA-mediated down-regulation of HIF-1 alpha can be used to inhibit angiogenesis, in particularly in diseases such as diabetic retinopathy, age related macular degeneration and many types of cancer.

WO 2004/042024 A2



---

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*